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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.              | CONFIRMATION NO.       |
|--|-------------|----------------------|----------------------------------|------------------------|
| 10/510,469   | 10/07/2004  | David Gene Barrett   | PU4724USW                        | 6905                   |
| 23347 7590 09/19/2007<br>GLAXOSMITHKLINE<br>CORPORATE INTELLECTUAL PROPERTY, MAI B475<br>FIVE MOORE DR., PO BOX 13398<br>RESEARCH TRIANGLE PARK, NC 27709-3398 |             |                      | EXAMINER<br>NOLAN, JASON MICHAEL |                        |
|  |             |                      | ART UNIT<br>1626                 | PAPER NUMBER           |
|  |             |                      | MAIL DATE<br>09/19/2007          | DELIVERY MODE<br>PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

10/510,469

**Applicant(s)**

BARRETT ET AL.

**Examiner**

Jason M. Nolan, Ph.D.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-46, 49 and 50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 43-46, 49 and 50 is/are rejected.
- 7) ☒ Claim(s) 3-42 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 10/07/2004.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

**Claims 1-46, 49 & 50** are pending in the instant application; of which, **Claims 14-25, 27-42, 44-46, 49 & 50** are currently amended. **Claims 47 & 48** are canceled.

#### *Information Disclosure Statement*

The information disclosure statement filed 10/07/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 1, 2, 43-46, 49 & 50** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of the formulae (I) & (II) and a salt or solvate thereof, is not enabled for *physiologically functional derivatives* thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

### ***The Nature of the Invention***

The nature of the invention is the compounds of formulae (I) & (II), including a salt or solvate thereof, and *physiologically functional derivatives*. The term “physiologically functional derivatives” is defined on pages 14-15 in the instant specification and encompasses *any* pharmaceutically acceptable derivative of a compound of formulae (I). Said derivatives would include esters, amides, metabolites, prodrugs, polymorphs, etc. To demonstrate the lack of predictability for derivatizing an organic compound, and therefore enablement, polymorphs are discussed below.

### ***The state of the prior art and the predictability or lack thereof in the art***

Active pharmaceutical ingredients (APIs) are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact and generally stable format to store an API or a drug product. Understanding and controlling the solid-state chemistry of APIs, both as pure drug substances and in formulated products, is therefore an important aspect of the drug development process. APIs can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms such as polymorphs and solvates are not so common as to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them and evaluate their properties as valuable new pharmaceutical materials. A large number of factors can influence crystal nucleation and growth during this process, including the composition of the crystallization medium and the processes used to generate supersaturation and promote crystallization, (Morissette *et al.* Advanced Drug Delivery Reviews **2004**, 56, 275-300).

For instance, the phenomenon of polymorphism, in the crystallization of organic compounds, is of crucial importance to the pharmaceutical industry. Two polymorphs of the same drug molecule may have different physical properties: e.g. solubility, bioavailability, melting points, density, hardness, or color; and may have dramatically different properties that effect the scale-up process. Due to the differences between polymorphs, the drug regulatory authorities (e.g. the FDA) are increasingly demanding more information about potential drug products before granting approval. The conditions under which polymorphs interconvert is also of crucial importance, particularly when drugs may encounter exposure to changes in temperature, pressure, and relative humidity during processes such as drying, granulation, milling, compression, and storage. Therefore, for these reasons, *the state of the prior art is*

*one of unpredictability.* The science of crystallization has evolved such that said differences in properties implies patentable distinctiveness between polymorphs.

***Amount of direction/guidance & presence or absence of working examples***

The direction or guidance present in the instant specification for the preparation of *physiologically functional derivatives* for the compounds of formula (I) is found on page 14 of the specification, lines 26-32. Typical salts for pharmaceutical formulation are listed on page 27. However, there are no working examples present in the disclosure. Therefore, one of skill in the art would be required to identify what type of derivative to make for each compound and, further, identify where on each molecule to make the functional group adjustment in order to determine what is being claimed.

***The breadth of the claims***

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any derivative of formula (I).

***The quantity of experimentation necessary***

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any derivatives, of a compound of formulae (I) & (II) as instantly claimed. The science of crystallization, for example, has not evolved such that without guidance or working examples in the

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specification, the claims lack enablement. This rejection can be overcome by deletion of the term *physiologically functional derivatives* from **Claims 1, 2, 43-46, 49 & 50**.

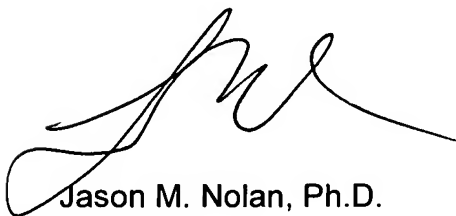
### ***Claim Objections***

**Claims 1 & 2** are objected to because of the following informalities: there are two variables defined as "m". Examiner suggests changing the second one to "t". Appropriate correction is required.

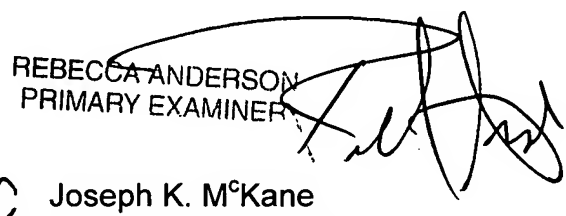
**Claims 3-42** are objected to as being dependent upon a rejected base **Claim 1**, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M<sup>c</sup>Kane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Jason M. Nolan, Ph.D.  
Examiner  
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REBECCA ANDERSON  
PRIMARY EXAMINER

Joseph K. M<sup>c</sup>Kane  
Supervisory Patent Examiner  
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Date: September 15, 2007